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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/043,539	01/11/2002	Ambrose L. Cheung	DC-0199	7285

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/043,539	CHEUNG ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: _____.

DETAILED ACTION

Claims 28 and 30 are pending; claims 29 and 31 have been canceled.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

2. The information disclosure statement filed January 12, 2006 has been considered.

Withdrawn Rejections

3. Rejections over canceled claims are automatically withdrawn.

4. ***Withdrawn Rejection Claim Rejections - 35 USC § 101.*** Claims 30-31 are directed to compounds that have not been isolated and purified to show the "hand of man" and are therefore directed to non-statutory subject matter. This rejection was obviated by amending the claim 30 to recite the phrase ----isolated and purified---- and cancellation of claim 31.

5. ***Withdrawn Rejection,*** Claim 29 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is herein withdrawn in light of the cancellation of the claim.

Response to Arguments

6. Applicant's arguments filed January 12, 2006 have been fully considered but they are not persuasive.

7. **Rejections Maintained** ***Double Patenting:*** The rejection of claim 30 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 1 of U.S. Patent No. 5,587,288 is traversed on the grounds that at page 32, lines 22-25 the instant Specification teaches that SarR down regulates sarA expression by binding to the sarA promoter to down modulate sarA transcription.

8. It is the position of the examiner that at paragraph [0147], sarA locus is auto regulated by the SarA protein: "One class of transcription-activating proteins bears two structural motifs, namely a DNA binding and an activation domains (52). The SarR protein was initially defined as a transcriptional repressor protein that binds the sarA promoter region (39), thus leading to reduced transcription from the sarA P1 promoter. As stated previously, the sarA P1 promoter is the predominant promoter in the sarA regulatory system. Transcriptional fusion studies indicate that the sarA locus is auto-regulatory (21), possibly mediated by the binding of SarA to its own promoter. The binding affinity of SarR to a sarA promoter fragment is higher than its SarA counterpart (40), consistent with the idea that an activation motif might be present on the SarA protein but not on the SarR protein, and that SarR may repress by a simple competitive displacement mechanism. A second possibility is that SarA and SarR may form a hetero-dimer to interfere with the function of the SarA homo-dimer. Due to the conservation of residues involved in the dimerization, this could happen in vivo. Finally, SarR may function similarly to the bacteriophage lambda repressor (which also has a helix-turn-helix DNA binding motif). In this case, a slight DNA binding site difference (one base pair shift) could turn an activator to a repressor by affecting the RNA polymerase binding (7)."

Therefore SarA is an analog of SarR protein (see sequence alignment, 30 % best sequence similarity) that can serve to autoregulate sarA, inhibit, sarA expression. The rejection is also being because the composition of claim 30 need not evidence any specific biological structure or function but must only be identified by the screening method, the identification not requiring any specific activity. The composition of claim 30 is defined by a recited intended use "A pharmaceutical composition" and product by process limitations "identified by the screening method of claim 28". In light of the fact that claim 28 does not comprise an identifying step, the compound of claim 30 must only be identified as a possible analog of SarR protein in the obtaining step and the allowed species of invention is an analog of SarR protein, specifically an SarA protein with a conserved amino acid sequence and will inhibit expression Staphylococcus

virulence determinants and therefore could serve the recited intended use of claim 30, that being a "pharmaceutical composition".

9. ***Objection Maintained: Specification*** The disclosure objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. At page 30, the phase www.tiger.org is recited. This phrase must be removed. While Applicant submitted an amendment of page 24 to remove the hyperlink, the hyperlink on page 30 of the instant Specification submitted to the USPTO has not been removed. Any additional hyperlinks present in the instant Specification also must be removed.

1. ***Rejection Maintained, Claim Rejections - 35 USC § 112(written description)*** Claims 28 and 30 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the *written description* requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention,

is traversed on the grounds that the claims have been amended to recite the phrase "a SarR protein having an amino acid sequence comprising SEQ ID NO 1".

2. It is the position of the examiner that SEQ ID NO1 is not an amino acid sequence, but a nucleotide sequence, therefore the newly submitted combination of claim limitations is not consistent with accepted nomenclature for what represents an amino acid sequence . No amino

acid sequences that comprise a nucleotide sequence of SEQ ID NO 1 are disclosed in the instant Specification.

3. Applicant further traverses the lack of written descriptions applied against claims 28 and 30 by asserting that Applicant has provided the crystal structure of a SarR homodimer, wherein SarR in Figure 11 is labeled with either an "H" when amino acid residues are involved in dimerization and labeled "D" when involved in DNA binding. Applicant also states that the "instant Specification provides a general description as to the how to use molecular modeling of a SarR protein having an amino acid sequence of SEQ ID NO 1."

4. It is the position of the examiner that what is obtained and is not a know SarR protein encoded by SEQ Id NO 1, not an SarR protein with the amino acid sequence of SEQ ID NO 2, but "one or more Staphylococcal regulatory R analogs that differ from the SarR protein encoded by SEQ ID NO 1, or evidences the amino acid sequence of SEQ ID NO 2.

Analogs differ from a reference molecule

(DEFINITIONS PROVIDED BY THE INSTANT SPECIFICAITON: The instant Specification defines the SarR analogs to include SEQ ID NO 1, analogs of SEQ ID NO 1, homologs of SEQ ID NO 1 (see Instant Specification page 12, third paragraph on page), mutant polypeptides encoded by mutant sarR genes (see Instant Specification, page 5, last paragraph), wherein the homologs are compounds that "possess a "common evolutionary origin" including proteins from superfamilies and homologous proteins from different species. Such proteins have sequence homology as reflected by their high degree of sequence similarity (see Instant Specification page 10, last paragraph), as well as applies to "bacteria having significant sequence, structural or functional homology to the sarR gene or SarR protein" (see Instant Specification page 11, last few lines of first paragraph on page). Additionally, at page 13 of the Instant Specification the SarR analogs are defined to be "in the form of small molecule compounds which alter the functionings of a microbial sarA expression", the small molecules being obtainable by screening a random peptide library or chemical library (see Instant Specification , page 16, paragraph 2), and the SarR analogs of the claimed method and the pharmaceutical composition differ from SEQ ID NO 2 SarR, by any number of changes. The lack of written description was over the genus of claimed compositions that have only been claimed or described by a function and no structure, and a lack of a

representative number of species to claim a genus of pharmaceutical compositions that comprise compounds that have not yet been identified.

The examiner acknowledges the showing provided by Applicant in Figure 11, but what is now claimed is a method and compositions that DO NOT utilize the SarR protein of Figure 11, but analogs thereof, the sequences and structures of which are not known.

The lack of written description over the claimed pharmaceutical compositions of claim 30, identified by the method of claim 28, from which claim 30 depends is maintained for reasons for record and responses set forth above.

10. ***Rejection Maintained*** Claim 30 rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to SarR protein from Staphylococcus aureus, epidermidis, haemolyticus and saprophyticus. See M.P.E.P. §§ 706.03(n) and 706.03(z), is traversed on the grounds that Applicant's have provided the crystal structure of SarR and SarR analogs from S. epidermidis, S. haemolyticus and S. saprophyticus and one of skill in the art could envision and produce Sar R mutants without undue experimentation in view of the teachings of Topham et al.

5. It is the position of the examiner that the claim 30 is not limited to any specific analogs of SarR protein from S. epidermidis, S. haemolytic or S.saprophyticus, nor is it limited to mutations at any specific locations within a reference sequence (SEQ ID NO 2). The instant Specification proposes to identify small molecules and other analogs from chemical libraries that would serve to bind to and inhibit expression of sarA in Staphylococcus. A proposed method of identifying, possible locations for making changes does not describe a molecule that will form a heterodimer

with SarA which in turn will function as a pharmaceutical composition. While a person of skill in the art may be able to make analogs of SarA of SEQ Id NO 2, the instantly claimed highly variable genus of analogs that would serve as a pharmaceutical composition has not been described (see written description rejection of record), and what has not been described has not been enabled, despite the fact that a person of skill in the art could make analogs, the ability of the analog to treat or prevent Staphylococcal infection and disease is unpredicatable in the art of vaccines, and thus the function of the analog as a pharmaceutical composition is not evident until the analog is actually tested and evaluated in vivo or an art recognized in vitro method. The instant Specification does not show or nor provide guidance on how *any SarR analog* could or would function as a pharmaceutical composition when the changes from the reference SarR protein sequence may be any number of changes. The scope of enablement is maintained for reasons of record, and responses set forth above.

6. ***Claim Rejections - 35 USC § 102*** Claim 30 rejected under 35 U.S.C. 102(a) as being anticipated by Tegmark et al (2000) is traversed on the grounds that:

claim 29 has been canceled rendering the rejection mute.

7. It is the position of the examiner that claim 30 is still pending and no evidence has been made of record to show the SarR analog of Tegmark et al would not function as an isolated and purified compound composition. The rejection of claim 30 is maintained for reasons of record.

Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or

of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. AThe Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art≅.

8. ***Rejection Maintained***:Claim 30 rejected under 35 U.S.C. 102(b) as being anticipated by Manna et al (1998) in light of evidence provided by Manna et al (2001) is traversed on the grounds that claim 29 has been canceled, and the rejection should therefore be withdrawn.

9. It is the position of the examiner that claim 30 is still pending and no evidence has been made of record to show the SarR analog of Manna et al would not function as an isolated and purified compound composition. The rejection of claim 30 is maintained for reasons of record.

Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

10. **Rejection Maintained**: Claim 30 rejected under 35 U.S.C. 102(e) as being anticipated by Hurlburt et al (US Pat. 6,699,662 B1) is traversed on the grounds that "the reference does not

teach or suggest a SarR analog of a SarR protein having an amino acid sequence comprising SEQ ID NO 1 or heterodimer formation of the SarR analog with SarA to inhibit expression of sarA of staphylococcus.

It is the position of the examiner that no evidence was made of record to show the isolated and purified compound of Hurlburt et al would not function as a pharmaceutical composition. The rejection of claim 30 is maintained for reasons of record.

New Grounds of Rejection/Objection

New Objection to the Specification

10. The disclosure is objected to because of the following informalities: The Amendment of page 24, starting at line 28 does not correspond to the disclosure of the Specification submitted as originally filed. The Objection to the Specification for a hyperlink was made with respect to disclosure set forth on page 30 of the instant Specification. The amendment of page 24 should be page 30. Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. Claims 28 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Original descriptive support for SarR protein that comprise the polynucleotide sequence of SEQ ID NO 1 could not be found in the instant Specification. Therefore, claims 28 and 30 recite a combination of claim limitations that are NEW MATTER.

11. Claims 28 and 30, as amended, recite terminology that is contrary to its ordinary meaning, the written description must clearly redefine the claim terms and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "SEQ ID NO 1" (a nucleotide sequence) in claims 28 and 30 is used by the claim to mean "amino acid sequence", while the accepted meaning is "a nucleotide coding sequence for a open reading frame or gene sequence." The term is indefinite because the specification does not clearly redefine the term.

12. Claim 30 recites the limitation "compound identified" in reference to claim 28 which recites the methods steps of obtaining, contacting and determining the formation of a heterodimer and does not identify any compounds. There is insufficient antecedent basis for this limitation in the claim. Claim 28 does not claim a methods step of identifying the compound in the heterodimer complex.

Double Patenting

13. Claim 28 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 22 of copending Application No. 11/063308. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims are directed to methods that determine the formation of heterodimers in a method of screening for lead compounds which inhibit expression of sarA in Staphylococcus. The methods determine the formation of heterodimers and therefore must obtain and contact SarA with an analog with a compound that could form a heterodimer in order to determine heterodimer formation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

14. Claim 30 is rejected under 35 U.S.C. 102(e) as being anticipated by Doucette-Stamm et al (US Pat. 6380370, SEQ ID No 4993, filing date August 13, 1998).

1. Doucette-Stamm et al disclose the instantly claimed invention directed to a composition that comprises an isolated and purified compound that is an analog of SEQ ID NO 2, or an analog encoded by SEQ ID 1, the Staphylococcal polypeptide compound of Doucette-Stamm et al shares 84.2% sequence identity with SEQ ID NO 2, and is therefore an analog of SarR obtained from Staphylococcus with the recited intended use as a therapeutic (see title). The composition anticipates the instantly claimed invention as now claimed. Sequence alignment provided herewith.

2. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

3. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not

recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Conclusion

15. This is a Non-Final action.

16. The prior art considered pertinent to applicant's disclosure.
- US006020121A is cited to show a method of screening for sar gene regulator inhibitors (see claim 9).
- US005976792A is cited to show P1, P2, and P3 promoters of sarA (see Figure 7).
- US 20040147734A1 is cited to show Staphylococcus epidermidis polypeptides.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
April 12, 2006

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